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# PERSONALIZED MEDICINE AND *COMPLEXIO* “WHAT IS HUMAN?” AS A MEDICAL QUESTION\*

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## ABSTRACT

In this paper, I show the parallelism between the Galenic concept of “complexion” (*complexio*, in Latin) as it was used in the medieval medical and natural-philosophical texts and the current concept of “personalized medicine”. In this way, I point out to what extent the parallelism between personalized medicine and the medieval notion of “complexion” is nowadays relevant to inquire the *proprium* of the “human” in a bio-medical framework. For, the medieval notion of “complexion” as “substantial quality” optimally worked as to deal with the problem of reconciling the “case-by-case” approach of medicine with the need of a unified bio-medical account of the “human”. Against the background of this reasoning, I further suggest that a mesoscopic perspective on the living organisms, as the one entailed by the concept of “complexion” and used in current scenarios of Systems Biology, could be advantageous to the bio-medical investigations on “what is human”.

## KEYWORDS

Complexion, personalized medicine, human, substantial quality, mesoscopic perspective.

## 1. INTRODUCTION: PERSONALIZED MEDICINE FROM A HISTORICAL PERSPECTIVE

In recent years, the concept of “Personalized Medicine” (PM) has acquired a central place in medical literature. The definition of PM is in itself controversial and widely debated. The connection between “personalization” and genotype is easy to follow given that the biological genetic paradigm still dominates today and that knowledge about the genes of a patient is, to some extent and for certain diseases, useful for tailoring treatment to the patient’s condition. In a broader sense, however, “personalizing medicine” means considering the variability of the human body in itself and in relation to its context in order to make diagnoses and treatments that are the most fitting and effective for the individual patient. This second,

\* I thank prof. Marta Bertolaso, prof. Alfredo Marcos, and dr. Alessandro Giuliani for their comments on an earlier draft of this paper. I also thank prof. Céline Lafontaine for her useful remarks.

broader sense of PM touches upon an evident fact: each patient is a complex system with all his/her idiosyncrasies, co-morbidity, intolerance profile, metabolism, and psychological attitude.<sup>1</sup>

Scholarship has not ignored the antecedents in pre-modern science and medicine of this broader conception of PM. Yet, although some references to ancient and early-modern medicine can be found in the current literature,<sup>2</sup> a precise history of PM has not been retraced. The longevity of the old question “Is medicine a science or an art?” and the fact that “personalization”, “particular”, and “individual” are already implied in the concept of medicine as “τέχνη” or “ars” both suggest the continued relevance of retracing a comprehensive history of PM. It should be further noted that the medieval period has been particularly overlooked with regard to the history of PM, despite the fact that medieval scientific texts preserve a rich body of medical theories and practices in line with the theoretical premises of PM. Avicenna’s famous position on the difference between philosophy and medicine is one clear example. According to Avicenna, philosophical knowledge is based on ultimate principles, while medical expertise is based on sense observations of particular situations. In controversial cases in which the natural-philosophical and the medical traditions held opposite views on milestones in human biology (such as sensation, nutrition, and reproduction), the different views of philosophers and physicians were ascribed to their respective ways of looking at living organisms. The philosophical way is led by rational reasoning that goes beyond sensation and grasps the first causes of the phenomena, while the medical way is guided by sense experience that adheres to phenomena.<sup>3</sup> Thus, the latter way, i.e. the viewpoint of nature proper to the medical domain, already implies a

1 The literature on PM is vast. I list a few contributions that deal directly with the definition of PM: J. Schildmann and J. Vollmann, “Personalized Medicine: Conceptual, Ethical, and Empirical Challenges”, in: T. Schramme, S. Edwards (eds.), *Handbook of the Philosophy of Medicine*, Springer, Dordrecht 2017, pp. 903-913; X. Guchet, *La médecine personnalisée. Un essai philosophique*, Les Belles Lettres, Paris 2016; A. Gamma, “Personalized and Precision Medicine”, in: M. Solomon, J. R. Simon, H. Kincaid (eds.), *The Routledge Companion to Philosophy of Medicine*, Routledge, Taylor & Francis Group, London 2016, pp. 397-407; W.K. Redekop and M. Mladsi, “The Faces of Personalized Medicine: a Framework for Understanding its Meaning and Scope”, *Value in Health: The Journal of the International Society of Pharmacoeconomics Research*, 16,6 Suppl., 2013, pp. S4-S9; S. Shleiden et alii, “What is Personalized Medicine: Sharpening a Vague Term Based on a Systematic Literature Review”, *BMN Medical Ethics*, 14, 55, 2013, pp. 1-12; K. K. Jain, *Textbook of Personalized Medicine*, Springer, Dordrecht 2009.

2 See E. Abrahams and M. Silver, “The History of Personalized Medicine”, in E. Gordon and S. Koslow (eds.), *Integrative Neuroscience and Personalized Medicine*, Oxford University Press, Oxford 2010, pp. 3-16. In 2014, a conference has been organized at John Hopkins University with the title “Individualized Medicine in Historical Perspective. From Antiquity to the Genome Age” (<https://www.hopkinshistoryofmedicine.org/content/international-conference-history-individualized-medicine>).

3 See J. Chandelier, “Medicine and Philosophy”, in H. Lagerlund (ed.), *Encyclopedia of Medieval Philosophy. Philosophy between 500 and 1500*, Springer, Dordrecht 2011, pp. 735-742.

strong idea of personalization and assumes that the physician’s sight should be oriented towards the particular condition of the patient observed by the senses.<sup>4</sup>

In my view, the clearest opportunity for retracing a history of personalized medicine in the Middle Ages lies in the concept of “complexion”. In the following section, I show the clear-cut parallelism between PM and the medical view coming from the concept of “complexion” (*complexio* in Latin) as it was used in medieval medical and natural-philosophical treatises.<sup>5</sup>

## 2. PERSONALIZED MEDICINE AND *COMPLEXIO*

*Complexio* (“κρᾶσις” in Ancient Greek) is one of the pivotal concepts in Galen’s medical theory. It is the balanced blend of the primary qualities (hot, cold, wet, and dry) that results from the mixture of the primary elements (earth, air, water, and fire)<sup>6</sup>. Since Galen incorporated the Hippocratic idea of “humors” into

4 A reference to what has been called “Avicenna’s personalized medicine” is found in R. Moeini et alii, “Historical Root of Precision Medicine: An Ancient Concept Concordant with the Modern Pharmacotherapy”, *DARU Journal of Pharmaceutical Science*, 27, 7, 2017, pp.1-2. The literature on the problem of medicine considered as an art/science and on the tension between medical doctrine and medical practice is vast, especially for Scholastic medicine. I mention only one book that directly addresses the issue of the individual/universal in medieval medicine: R. Cardini and M. Regoliosi (eds.), *Umanesimo e Medicina. Il problema dell’individuale*, Bulzoni, Roma 1996 and especially the contribution by Chiara Crisciani within that volume: C. Crisciani, “L’individuale nella medicina tra Medioevo e Umanesimo. I ‘Consilia’”, pp. 1-32.

5 Maaïke van der Lugt has already presented two papers (to my knowledge, unpublished to date) on the link between personalized medicine and complexion: “Individuality, Complexion, and the Limits of Personalized Care in Medieval Medicine” presented at the John Hopkins conference mentioned in footnote 3 above and “Individual Complexion and Personalized Care in Medieval Medicine” presented at the University of Cambridge in 2017 (<http://talks.cam.ac.uk/talk/index/85341>).

6 On the late medieval concept of “complexion” see especially L. Thorndike, “De Complexionibus”, *Isis*, 49, 1958, pp. 398-408; N. G. Siraisi, *Medieval and Early Renaissance Medicine*, The University of Chicago Press, Chicago 1990, pp. 101-104; P.-G. Ottosson, *Scholastic Medicine and Philosophy. A Study of Commentaries on Galen’s Tegni* (ca. 1300-1400), Bibliopolis, Napoli 1984, pp. 127-194; Michael R. McVaugh, *Arnaldi de Villanova Opera Medica Omnia, II, Aphorismi de gradibus*, Universitat de Barcelona, Barcelona-Granada, 1975, pp. 9-10 and pp. 20-22; G. Zanier, “Il problema della complexio e la nozione del vivente in Marsilio di Inghen”, *Esercizi Filosofici/Testi*, VI, 2002, pp. 69-77; V. Groebner, “Complexio/Complexion. Categorizing Individual Nature. 1250-1600”, in L. Daston and F. Vidal (eds.), *The Moral Authority of Nature*, The University of Chicago Press, Chicago 2004, pp. 361-383. The history of the translation of the word/concept of κρᾶσις into the Latin word/concept of “complexion” is not at all a linear one, as Danielle Jacquart has described in an article of 1984, see D. Jacquart, “De crasis à complexio: note sur le vocabulaire du temperament en latin médiéval”, in G. Sabbah (ed.), *Textes médicaux latins antiques*, Publications de l’Université de Saint-Etienne, Saint-Etienne 1984, pp. 71-76. And there is not a unique definition of the concept of “complexion” emerging from medieval texts. I took here the definition of “complexion” as given by Joel Kaye in his book *A History of Balance* of 2014, with some minor

his medical theory, the concept of “complexion” is also linked to the balance of blood, yellow bile, black bile, and phlegm<sup>7</sup>. The concept of “complexion” forms the idea of “health” as a balanced state of the body and its parts. In other words, a balanced complexion implies bodily health, while an imbalance causes a pathological condition in the organism. The Galenic concept of complexion appeared in the Latin cultural milieu through the translations of Galen’s works and through the mediation of the Arabic sources<sup>8</sup>; it played an important role both in medical theories and in medical treatments. As far as the medieval medical theorists were concerned, the concept of “complexion” was incorporated into reflections on living organisms, especially in commentaries on Galen. The concept of complexion was also used in other conceptual frameworks, such as natural philosophy or theology. As far as natural philosophy is concerned, *complexio* appears in commentaries on Aristotle’s *De generatione et corruptione* (i.e., philosophical texts that discuss primary qualities and elements) and in more strictly biological texts, like commentaries on Aristotle’s *De anima*, *Parva naturalia*, and *De animalibus*<sup>9</sup>.

In late medieval medicine and natural philosophy, complexion was conceived as a comparative and relational entity. Not fixed nor immutable, complexion was relativized according to the internal and external conditions of a singular species, an individual body, and a particular organ; a perfectly balanced complexion was thought impossible to find in nature. The underlying idea was that the elements and humors in the body were configured for *each* individual organism and in a peculiar and nonreplicable way in each instance. In the wake of Galen and Avicenna, late medieval scientists discussed complexion in terms of *temperamentum ad pondus* and *temperamentum ad iustitiam*. The *temperamentum ad pondus* is a perfectly tempered complexion as it is an absolute average between qualities and

changes, see J. Kaye, *A History of Balance, 1250-1375. The Emergence of a New Model of Equilibrium and its Impact on Thought*, Cambridge University Press, Cambridge, 2014, pp. 128-240.

7 Note that the word “complexion” and the word “temperamentum” mostly overlapped in medieval scientific literature. However, “complexion” was usually used as a more technical term referring to the mixture of qualities, while “temperamentum” was most often referred to the humoral blend.

8 The concept of “complexion” appeared in the Latin cultural milieu especially through the mediation of Avicenna’s *Canon* and Averroes’s *Colliget*, through the Pantegni, and through the translation of the *Περὶ κρᾶσεων* into the Latin *De complexionibus* by Burgundio of Pisa in the late Twelfth century.

9 The use of the concept of “complexion” in the natural-philosophical and theological traditions has been overlooked in scholarly literature. The concept of “complexion” in natural-philosophical texts have been addressed by some of the authors quoted in footnote 7 above and 11 below. A recent conference organized in Cluj gathered experts in the history of philosophy discussing the theory of humors and the concept of “complexion” also under natural-philosophical respects. The conference was titled “Medicine and Philosophy. The *longue durée* of the humoral theory” and took place on May 10-11, 2019. Within the same conference, also a paper on the use of the concept of “complexion” in theological writings has been presented, i. e., Gabriella Zuccolin, “Thomas Aquinas on Bodily Complexion”.

so an optimally-blended mixture. The *complexio temperata ad pondus* lays at a supposedly precise middle point in a theoretical continuum between two extreme primary qualities. It was also defined as a *complexio per intellectum*, entailing the idea of something never found in nature and posited on a purely theoretical level. The elements and humors of the *temperamentum ad iustitiam*, on the other hand, are not disposed in a static and invariant configuration that is perfectly balanced according to a precise measurement. The *temperamentum ad iustitiam* always requires the concept of "proportion". The humors of the *temperamentum ad iustitiam* are configured proportionally and in the way most suitable for a particular organ, single organism, or natural species to operate in a given situation. This means that health is the result of a state of the humors whose proportions vary from case to case. And this is why "health" was often defined as an "adjustment" of the humors *ad iustitiam*. The *complexio temperata ad iustitiam* was also called "real" (*realis*); for only a proportioned rather than an exact (*punctualis*) configuration of the humors can actually be applied to natural entities. However, medieval authors often described the balance (or imbalance) of organisms in terms of *complexio lapsa* (where *lapsa* means "fallen"). The proportioned adjustment of humors, which guarantees an organism's health, is the balance that medieval physicians aimed to realize. But the reality of nature is always different. In nature we find *complexiones lapsae*, i.e. non-tempered complexions that deviate from an ideally balanced complexion. This also explains why medieval authors often talked about complexions in terms of *complexiones respectivae*; physicians and natural philosophers of the late Middle Ages theorized that a complexion occurring in nature, in order to be deemed more or less balanced, and therefore the most healthy and long-lasting, must always be compared to the *complexio temperata ad iustitiam*, taken as the archetypical complexion. Complexions are *respectivae* also because the complexion of an organism or an organ cannot be called "balanced" or "healthy" without being compared to the complexions of other species or organs. In general, the absence of naturally occurring, perfect complexions makes it impossible to describe the best complexion or which complexion would guarantee the longest life expectancy. Several contingent conditions, both external and internal to the organism, can affect humoral configuration and influence health conditions. As a consequence, the physician must endeavor to cure the imbalance of a particular complexion in order to obtain the best possible condition for the individual patient.<sup>10</sup>

This overview has shown the main traits of the comparative and relational conception of "complexion" held by medieval scientists. The ideas of "health" and

10 See D. Jacquart, *La médecine médiévale dans le cadre parisien, XIVe-XVe siècle*, Fayard, Paris 1998, pp. 391-402; C. Beneduce, "John Buridan on Complexion. Natural Philosophy and Medicine in the Fourteenth Century" in: C. Beneduce and D. Vincenti (eds.), *Oeconomia corporis. The Body's Normal and Pathological Constitution at the Intersection of Philosophy and Medicine*, MEFISTO Supplement 7, ETS, Pisa 2018, pp. 41-49.

“disease” entailed in this view on bodily constitution immediately recall the underlying inspiration for the contemporary trend of “personalized medicine”. A physician’s evaluation must consider the special conditions that pertain to or affect a particular patient. Nowadays, this especially applies to cancer, neurodegenerative, and autoimmune diseases. Since cancer, neurodegenerative, and autoimmune diseases are nonlinear, systemic, multi-level pathologies that lack strict criteria for measurement and indexing,<sup>11</sup> a personalized approach to diagnosing and treating such complex pathologies is especially appealing to researchers and clinical practitioners in these respective medical fields. By and large, the theoretical framework shared by PM and medieval theories on complexion seems to be as follows: medicine works better with particulars than with universals; it is based on sense observation of individual situations; and it does not rely upon overly generalizing principles. In other words, this framework appears to be a reformulation of Avicenna’s medical approach to nature, i.e., that medicine is not oriented towards universal principles and first causes but should take into account the complexity of reality observed in individual cases.

### 3. PERSONALIZED MEDICINE AND THE NOTION OF “HUMAN”

Medicine and PM in particular focus on individual cases and take into account bio-medical variables in bodily constitution, affected organs, and states of health and illness. One possible consequence of this approach is that any universal notion of “human” loses all meaning as regards the realm of bio-medicine. However, we regularly qualify diseases, organs, and the body and other medical objects with the adjective “human”. So how can PM be compatible with a general notion of “human”? We may also expand the scope of the challenge by asking which directions bio-medicine and the bio-medical humanities should take in order to investigate the *proprium* of the “human”. Against the background of my parallelism between PM and pre-modern theories of complexion, I point out that medieval scientists tried to provide a definition of the “human” within discussions on *complexio*. Finally, I underline to what extent the parallelism between the medieval notion of complexion and PM may motivate new inquiries into bio-medical definitions of the human.

In the Late Middle Ages, physicians produced elaborate theories on complexion that also influenced how the human being and human nature were described

<sup>11</sup> In cancer, for example, the recognition of the different levels of the tumor microenvironment does not constitute a separation or isolation of each level but, on the contrary, an invitation to explore the complex dialogue between those levels. See M. Bertolaso, *Philosophy of Cancer. A Dynamic and Relational View*, Springer, Dordrecht 2016.

in a bio-medical domain.<sup>12</sup> In late medieval medicine, medieval scientists had to deal with the following problem: if the physician must consider the particularity of the individual body and individual, ever-differing complexions, how is it still possible to speak about the “human being” within a medical framework? In other words, medieval physicians had to find an interpretation of *complexio* that allowed them to keep the medical discourse focused on a general idea of “human” while at the same time retaining the character of variability distinctive to *complexio*. They solved the issue by describing complexion in terms of “substantial quality”.<sup>13</sup> Substantial quality is not a substance (the essence of the “human” as substantial form or soul); nor is it an accident (a merely contingent material occurrence within the human body). It is a property possessed by all human beings that is different in each person. Contrary to a substance, complexion as a substantial quality can be subject to variation. And contrary to an accident, complexion is a property that transverses all individual persons/patients. In the words of Joël Chandelier and Aurélien Robert:

... la complexion [,] se trouve précisément à l’interface entre la matière et la forme, entre la substance et l’accident, entre ce qui est purement corporel et ce qui appartient à l’âme. La notion de complexion permet ainsi de conserver l’unité de l’espèce humaine d’un point de vue métaphysique – tous les êtres humains ont la même forme substantielle – tout en acceptant une variation infinie de degrés dans la complexion – chaque individu a une complexion singulière, quoique toujours humaine.<sup>14</sup>

Furthermore:

De même, tous les hommes n’ont pas exactement la même complexion, mais tous ont une complexion proprement humaine qui varie selon le plus et le moins. Ainsi, bien que la complexion ne soit ni la substance de l’homme, ni son âme, elle est coextensive à l’humanité et indique quelque chose de sa nature, autrement dit de ce qui distingue l’homme des autres espèces naturelles.<sup>15</sup>

Complexion is therefore *coextensive* with humanity but is not an essence in itself and so justifies the variability implied in medicine. With this reading of the concept of complexion, medieval physicians managed the theoretical tension between the universality of the notion of “human being” and the individuality implied in their own conception of bodily constitution. This allowed them to make room for a general idea of “human nature” within their discipline, while maintain-

12 Most of my reconstruction in this section follows the article by J. Chandelier and A. Robert, “Nature humaine et complexion du corps chez les médecins italiens de la fin du Moyen Âge”, *Revue de synthèse*, IV, 134, 2013, pp. 473-510.

13 Chandelier and Robert reconstruct the historical-philosophical background for this concept, see J. Chandelier and A. Robert, cit., esp. pp. 480-485.

14 J. Chandelier and A. Robert, cit., 484-485.

15 J. Chandelier and A. Robert, cit., 482.



ing their conception of medicine based on a case-by-case perspective on each organism. More specifically, through their concept of “complexion” as substantial quality they shaped a medical reading of the *proprium* of the “human” that retained universal traits while being compatible with their individually-oriented medical theory and practice. In doing so, they succeeded in binding the unity and universality of the “human” with the multiple possibilities of its manifestations and variations.<sup>16</sup>

The triumph of PM that accompanies today’s bio-medical sciences presents us with an analogous scenario. Philosophers and medical scientists are faced with the similar challenge of constructing a concept of the “human” that works within the highly pluralistic and individually-oriented approach of modern medicine. However, the challenge of the twenty-first century is, at the same time, more difficult and more urgent. “Personalizing medicine” in our century is concomitant with an ever-increasing amount of medical information; the challenge posed by processing vast collections of medical data makes the need for common criteria in medical research and practice all the more apparent.<sup>17</sup> Along with these considerations, bio-medical scientists and philosophers of the life sciences would do well to continue to regard “what is human?” as a core research-question and not to underestimate the importance of making the case-by-case approach of PM compatible with a unitary notion of “humanity”.

In pursuing this aim, the medieval theory of complexion again appears to be an interesting and relevant case study.

In a certain sense, there is at least one evident difference between the respective challenges facing medieval and contemporary medicine. As mentioned above, medieval scientists elaborated upon the concept of “complexion” in terms of “substantial quality” and thus found a way to reconcile the general notion of “human nature” with the contingency of medical facts. However, that reconciliation seems to have held together more easily for them than it does in modern times. For medieval scientists had to deal with the problem of keeping a general notion of the “human” within a particulars-based science, *but* they had a strong theoretical touchstone at their disposal, namely, the universal notion of “human” as defined by the soul or the substantial form (as in the Aristotelian tradition). Their problem, then, was to characterize complexion such that it neither coincided with

16 Cf. J. Chandelier and A. Robert, cit., 476. The compatibility between a general notion of “human nature” and the unique individuality of each person had been the focus of Alfredo Marcos’ work: A. Marcos, “Sentido y diferencia. Una reflexión sobre el sentido de la vida humana en la era tecnocientífica”, *Pensamiento. Revista de investigación e Información filosófica*, 73, 276, 2017, pp. 425-444 and A. Marcos and M. Pérez, *Meditación de la naturaleza humana*, BAC, Madrid 2018. Marcos (2017) argues that the Aristotelian concept of “difference” could work as an interface between the general idea of “human nature” and the knowledge of each individual or concrete person.

17 On the problem of data related to in silico modeling and personalized medicine, see S. Green and H. Vogt, “Personalizing Medicine: Disease Prevention in silico and in socio”, *Humana. Mente Journal of Philosophical Studies*, 30, 2016, pp. 105-145.

that concept of human as "substantial form" nor collapsed under the quasi-infinite transience of the natural accidents. This becomes evident when we consider that medieval physicians had also to make their notion of *complexio* as a "substantial quality" compatible with the soul. How do the substantial form and the substantial quality of the body interact? Their solution ran as follows: the soul is received in matter on the basis of the degree of perfection of complexion which prepares the soul to be received by the body.<sup>18</sup> On the contrary, twenty-first century bio-medicine does not have a common theoretical framework with a clear notion of the "human". Modern bio-medical research lacks a strong philosophical idea or consensus on "what is human?"

Nevertheless, the parallel issues within the medieval theory of complexion and PM is still stimulatingly relevant to the modern-day bio-medical question of "what is human?" Medieval physicians described "complexion" as at the *interface* of form and matter, soul and body. It is a sort of *in-between structure* that allows them to keep the particular manifestations of medical facts unified under a transversal idea of "human being". Complexion as a quality emerges from particulars (the elements and the humors), without the particulars of the body being able to express that quality when isolated from one another. Complexion is the quality resulting from the integration of the elements and humors on a broader scale. In this sense, complexion emerges from matter, but it is not matter. At the same time, that more comprehensive scale in which the particulars are displayed is not the formal principle of the body in the same way as the soul is the substantial form of the body. For complexion is a mutable configuration, varying from person to person at different moments of the person's life. Contemporary research in bio-medicine and the bio-medical humanities would benefit from adopting a similar approach; that is to say, by searching for a characterization of the *proprium* of the human on a *mesoscopic* (middle-of-the-road) level of analysis. This is in fact an increasingly popular line of research in the bio-medical field of Systems Biology. Systems Biology adopts a holistic perspective on biology that considers living systems by integrating microscopic information into a more comprehensive scale. Moreover, Systems Biology argues that living systems cannot be understood only in terms of molecular biology; rather, the connection of molecular parts at a higher level is also required to grasp an organism's physiology and pathology. The theoretical idea of Systems Biology is that the sum of the parts generates a quality which is not possessed by any singular member of the system, such that the parts in isolation cannot reveal any relevant information of the living organism as a whole. Systems Biology thus seeks to connect in-between abstraction and biological evidence by studying "the gap between molecules and life",<sup>19</sup> the local and the

18 J. Chandelier and A. Robert, cit., p. 485.

19 F.C. Boogerd, F.J. Bruggeman, J.-H.S. Hofmeyer, H.V. Westerhoff (eds.), *Systems Biology. Philosophical Foundations*, Elsevier, Amsterdam 2007, p. 6.

global. Such mesoscopic (epistemological) perspective on living systems in very general terms means that biological explanations are to be framed not within the microscopic level of genes, proteins, or metabolites but at an intermediate position between the microscopic level and the macroscopic level of the organism.<sup>20</sup> Finally, the bio-medical question “what is human?” could be answered by adopting a systemic approach to the understanding of the human that entails relating both the microscopic and macroscopic. And the evidence seems to show that late medieval physicians were our forerunners in this regard.

#### 4. CONCLUDING SUMMARY

This paper shows the parallels between the medieval theory of complexion and some theoretical traits of contemporary personalized medicine. This allowed me to point out a crucial problem intrinsic to both frameworks: the need to reconcile the “case-by-case” approach of dealing with medical facts with a unified bio-medical account of “what is human?” Medieval physicians solved the problem by describing complexion as a “substantial quality”. Along this line of reasoning, I argued that a mesoscopic consideration of the living organism within the systemic framework of Systems Biology could be advantageous to bio-medical investigations of the “human”, looking at how impressively the medieval notion of complexion recalls us systemic nuances.

My reflection also suggested that a multidisciplinary humanistic perspective on personalized medicine, one that interlaces the history of philosophy and the philosophy of the bio-medical sciences, may yield new insights with regard to the concept of “personalized medicine” itself.

<sup>20</sup> See M. Bertolaso, A. Giuliani, L. De Gara, “Systems Biology Reveals Biology of Systems”, *Complexity*, 16, 6, 2011, pp. 10-16; S. Green (ed.), *Philosophy of Systems Biology: Perspectives from Scientists and Philosophers*, Springer, Dordrecht 2017; M. Bertolaso, A. Giuliani, S. Filippi, “The Mesoscopic Level and Its Epistemological Relevance in Systems Biology”, in A. X. C. N. Valente, A. Sarkar, Y. Gao (eds.), *Recent Advances in Systems Biology Research*, Nova Science Publishers, Hauppauge, NY 2014, pp. 19-36. New concepts in bio-medicine such as “morphogenetic fields” and “biological attractors” precedes in this direction. See M. Bertolaso and J. Dupré, “A Processual Perspective on Cancer”, in: D. J. Nicholson and J. Dupré (eds.), *Everything Flows, Towards a Processual Philosophy of Biology*, Oxford University Press, Oxford 2018, pp. 321-336; M. Bertolaso, *Philosophy of Cancer*, cit.